II. REMARKS

Formal Matters

Claims 15, 17, 18, 21, and 66 are pending after entry of the amendments set forth herein.

Claims 15 and 21 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. No new matter is added by these amendments.

Claims 16, 19, 20, and 67 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Examiner Interview

The undersigned Applicants' representative thanks Examiner Hutson and Examiner Achutamurthy for the courtesy of a telephonic interview, which took place on November 7, 2006 and which was attended by Examiner Hutson, Examiner Achutamurthy, Applicants' representative Paula A. Borden.

During the interview, the rejection of claims 15-17, 19-21, and 66 under 35 U.S.C.§ 112, first paragraph, was discussed. The amendments to the claims reflect the discussions which took place during the interview.

Rejection under 35 U.S.C.§112, first paragraph

Claims 15-17, 19-21, and 66 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking enablement.

The Office Action stated that the specification does not reasonable provide enablement for any screening assay for determining a candidate agent's DGAT modulatory activity, comprising contacting a DGAT polypeptide "having a mere 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:6" with a candidate agent and detecting any change in activity of the DGAT polypeptide compared to a control. Applicants respectfully traverse the rejection.

Claim 15 as amended recites an *in vitro* screening assay for determining a candidate agent's DGAT inhibitory activity, where the DGAT polypeptide used comprises an amino acid sequence having at least about 98% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:6.

The instant specification provides amino acid sequences of at least two mammalian DGAT polypeptides, and a nucleotide sequence encoding a plant DGAT polypeptide.

The specification describes a number of species of DGAT polypeptides. For example, the specification provides the amino acid sequence of a human DGAT polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6; and a mouse DGAT polypeptide comprising the amino acid sequence set forth in SEQ ID NO:7. Specification, page 9, lines 8-21. Thus, the specification provides at least two DGAT amino acid sequences. SEQ ID NO:6 and SEQ ID NO:7 share about 84% amino acid sequence identity.

Furthermore, the instant specification provides a nucleotide sequence, SEQ ID NO:4, encoding a plant DGAT. Specification, page 9, lines 21-24.

The instant specification provides ample description of how to determine DGAT activity.

The instant specification teaches how to determine whether an agent modulates DGAT activity. The specification provides a description of how to carry out a screening assay. Specification, page 21, line 18 to page 23, line 9. The specification provides a working example of how to measure DGAT activity. Specification, page 41, lines 10-21.

Given the guidance provided in the specification, combined with the knowledge in the art, those skilled in the art could carry out the claimed screening assay without undue experimentation.

The instant specification discusses structural features of DGAT polypeptides.

Structural features of DGAT polypeptides are discussed in the instant application. As discussed in the specification, there is a serine residue, which is also found in acylCoA:cholesterol acyl transferase (ACAT), that was reported to be important for ACAT activity, and is conserved in DGAT. Specification, page 39, lines 29-31; citing Cao et al. ((1996) *J. Biol. Chem.* 271:14642-14648). This conserved serine residue is depicted in Figure 2A of Cases et al. ((1998) *Proc. Natl. Acad. Sci. USA* 95:13018; a copy of which is was previously provided as Exhibit 1). The specification also notes that the carboxyl-terminal amino acid sequence is conserved. Specification, page 39, lines 25-27.

The specification further states that a DGAT polypeptide has hydrophobic domains and about 9 transmembrane domains. Specification, page 39, line 31 to page 40, line 5. These regions are indicated by a hydrophobicity plot, as depicted in Figure 2B of Exhibit 1.

Those skilled in the art could readily identify conserved residues and domains.

Those of ordinary skill in the art, given the DGAT amino acid sequences provided in the instant application, and given standard alignment software, could readily align the sequences and identify conserved

amino acids or regions. Those of ordinary skill in the art would know that conserved regions are generally less tolerant of change than non-conserved regions. For example, Bouvier-Navé et al. ((2000) *FEBS Lett.* 267:85-96; a copy of which is was previously provided as Exhibit 2) provides an amino acid sequence alignment of an *A. thaliana* DGAT, a *N. tabacum* DGAT, a putative human DGAT (referred to as "HsARGP"), a mouse DGAT, and a *C. elegans* DGAT. Exhibit 2, Figure 1. Exhibit 2 notes the hydrophobic domains, as discussed in the instant application. Exhibit 2, page 89, column 1, first full paragraph. Exhibit 2 further notes the presence of a conserved domain (AELLCFGDREFYKDWW). Exhibit 2, page 89, column 1, first full paragraph. Exhibit 2 notes the conserved serine discussed in the instant application. Exhibit 2, page 89, column 1, first full paragraph. Exhibit 2 further notes the presence of conserved arginine clusters. Exhibit 2, page 89, column 1, first full paragraph. Thus, those of ordinary skill in the art, given the amino acid sequences provided in the instant application, could readily identify conserved domains and residues, using nothing more than straightforward amino acid alignment.

Given the description in the specification, along with the knowledge in the art, those skilled in the art could readily practice the claimed invention without undue experimentation. As such, the instant claims comply with the enablement requirement of 35 U.S.C.§112, first paragraph.

Applicants submit that the rejection of claims 15-17, 19-21, and 66 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-105CIP2.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Dec. 21, 2006

By: _____
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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